IN THE UNITED STATES PATENT AND TRADEMARK OFFICE Sharp et al. Group Art Unit 1646 Appl. No. 09/782,816 I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Assistant Filed February 14, 2001 Commissioner for Patents, Washington, D.C. For PEPTIDE **INHIBITORS** OF May 30, 2001 CELLULAR **PROLIFERATION** Examiner Unknown

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, mailed on May 8, 2001, Applicants hereby request the entry of the substitute "Sequence Listing" submitted concurrently herewith into the specification, starting on a new page, immediately following the claims.

Kindly amend this application in the following aspects.

In the Specification:

Please replace the paragraph beginning at page 3, line 21, with the following rewritten paragraph:

--In one aspect, the invention concerns an isolated peptide selected from the group consisting of:

(X1), EVEKIKTTVKESATEEKLTPVXaaL(X2), (SEQ ID NO: 1),

(Y1)_nEVAALQVDRKVADEEKQSYDAV(Y2)_m (SEQ ID NO: 2),

wherein

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n and m independently represent 0 or 1, and Xaa is V or L;

X1 and X2 are independently defined as follows

X1 is GVKETPQQKYQRLLHEVQELTT (SEQ ID NO: 3), or

VKETPQQKYQRLLHEVQELTT (SEQ ID NO: 4), or

KETPQQKYQRLLHEVQELTT (SEQ ID NO: 5) or,

ETPQQKYQRLLHEVQELTT (SEQ ID NO: 6) or,

TPQQKYQRLLHEVQELTT (SEQ ID NO: 7) or,

PQQKYQRLLHEVQELTT (SEQ ID NO: 8) or,

QQKYQRLLHEVQELTT (SEQ ID NO: 9) or,

QKYQRLLHEVQELTT (SEQ ID NO: 10) or,

KYQRLLHEVQELTT (SEQ ID NO: 11) or,

YQRLLHEVQELTT (SEQ ID NO:12) or,

QRLLHEVQELTT (SEQ ID NO: 13) or,

RLLHEVQELTT (SEQ ID NO: 14) or,

LLHEVQELTT (SEQ ID NO: 15) or,

LHEVQELTT (SEQ ID NO: 16) or,

HEVQELTT (SEQ ID NO: 17) or,

EVQELTT (SEQ ID NO: 18) or,

VQELTT (SEQ ID NO: 19) or,

QELTT (SEQ ID NO: 20) or,

ELTT (SEQ ID NO: 21), or

LTT, or

TT, or

Τ;

and

X2 is AKQLAAL (SEQ ID NO: 22), or

AKQLAA (SEQ ID NO: 23), or

AKQLA (SEQ ID NO: 24), or

AKQL (SEQ ID NO: 25), or

AKQ, or

AK, or

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A;

and

Y1 and Y2 are independently defined as follows

Y1 is GEKETPVQKCQRLQIEMNELLN (SEQ ID NO: 26), or

EKETPVQKCQRLQIEMNELLN (SEQ ID NO: 27), or

KETPVQKCQRLQIEMNELLN (SEQ ID NO: 28), or

ETPVQKCQRLQIEMNELLN (SEQ ID NO: 29), or

TPVQKCQRLQIEMNELLN (SEQ ID NO: 30), or

PVQKCQRLQIEMNELLN (SEQ ID NO: 31), or

VQKCQRLQIEMNELLN (SEQ ID NO: 32), or

QKCQRLQIEMNELLN (SEQ ID NO: 33), or

KCQRLQIEMNELLN (SEQ ID NO: 34), or

CQRLQIEMNELLN (SEQ ID NO: 35), or

QRLQIEMNELLN (SEQ ID NO: 36), or

RLQIEMNELLN (SEQ ID NO: 37), or

LQIEMNELLN (SEQ ID NO: 38), or

QIEMNELLN (SEQ ID NO: 39), or

IEMNELLN (SEQ ID NO: 40), or

EMNELLN (SEQ ID NO: 41), or

MNELLN (SEQ ID NO: 42), or

NELLN (SEQ ID NO: 43), or

ELLN (SEQ ID NO: 44), or

LLN, or

LN, or

N; and

Y2 is VATVISTAR (SEQ ID NO: 45), or

VATVISTA (SEQ ID NO: 46), or

VATVIST (SEQ ID NO: 47), or

VATVIS (SEQ ID NO: 48), or

VATVI (SEQ ID NO: 49), or

VATV (SEQ ID NO: 50), or

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VAT, or

VA, or

V, and

derivatives thereof having at least about 90% identity with SEEQ ID NO: 1 or SEQ ID NO: 2.--

Please replace the paragraph beginning at page 5, line 31, with the following rewritten paragraph:

--In a preferred embodiment, the peptide has one of the following sequences: GVKETPQQKYQRLLHEVQELTTEVEKIKTTVKESATEEKLTPVXaaLAKQLAAL (SEQ ID NO: 51), where Xaa is as defined above, or

GEKETPVQKCQRLQIEMNELLNEVAALQVDRKVADEEKQSYDAVVATVISTAR (SEQ ID NO: 52), or has at least about 75%, preferably at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, most preferably at least about 95% identity with one of these sequences. Preferably, the peptide variants contain only conservative amino acid substitutions compared to the reference peptide sequences.--

Please replace the paragraph beginning at page 7, line 4, with the following rewritten paragraph:

--Figure 1 is the amino acid sequence of human p50 (SEQ ID NO: 53), wherein the peptide of SEQ ID NO: 51 (Xaa is L) is bolded and underlined.--

Please replace the paragraph beginning at page 7, line 6, with the following rewritten paragraph:

-- Figure 2 is the partial amino acid sequence of mouse p50 (SEQ ID NO: 54), wherein the peptide of SEQ ID NO: 51 (Xaa is V) is bolded and underlined.--

In the Claims:

Please amend the claims to read as follows:

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1(Amended). An isolated peptide selected from the group consisting of:

(X1)_nEVEKIKTTVKESATEEKLTPVXaaL(X2)_m (SEQ ID NO: 1),

(Y1)_nEVAALQVDRKVADEEKQSYDAV(Y2)_m (SEQ ID NO: 2),

wherein

n and m independently represent 0 or 1, and Xaa is V or L;

X1 and X2 are independently defined as follows

X1 is GVKETPQQKYQRLLHEVQELTT (SEQ ID NO: 3), or

VKETPQQKYQRLLHEVQELTT (SEQ ID NO: 4), or

KETPQQKYQRLLHEVQELTT (SEQ ID NO: 5) or,

ETPQQKYQRLLHEVQELTT (SEQ ID NO: 6) or,

TPQQKYQRLLHEVQELTT (SEQ ID NO: 7) or,

PQQKYQRLLHEVQELTT (SEQ ID NO: 8) or,

QQKYQRLLHEVQELTT (SEQ ID NO: 9) or,

QKYQRLLHEVQELTT (SEQ ID NO: 10) or,

KYQRLLHEVQELTT (SEQ ID NO: 11) or,

YQRLLHEVQELTT (SEQ ID NO:12) or,

QRLLHEVQELTT (SEQ ID NO: 13) or,

RLLHEVQELTT (SEQ ID NO: 14) or,

LLHEVQELTT (SEQ ID NO: 15) or,

LHEVQELTT (SEQ ID NO: 16) or,

HEVQELTT (SEQ ID NO: 17) or,

EVQELTT (SEQ ID NO: 18) or,

VQELTT (SEQ ID NO: 19) or,

QELTT (SEQ ID NO: 20) or,

ELTT (SEQ ID NO: 21), or

LTT, or

TT, or

Τ;

and

X2 is AKQLAAL (SEQ ID NO: 22), or

AKQLAA (SEQ ID NO: 23), or

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AKQLA (SEQ ID NO: 24), or

AKQL (SEQ ID NO: 25), or

AKQ, or

AK, or

A;

and

Y1 and Y2 are independently defined as follows

Y1 is GEKETPVQKCQRLQIEMNELLN (SEQ ID NO: 26), or

EKETPVQKCQRLQIEMNELLN (SEQ ID NO: 27), or

KETPVQKCQRLQIEMNELLN (SEQ ID NO: 28), or

ETPVQKCQRLQIEMNELLN (SEQ ID NO: 29), or

TPVQKCQRLQIEMNELLN (SEQ ID NO: 30), or

PVQKCQRLQIEMNELLN (SEQ ID NO: 31), or

VQKCQRLQIEMNELLN (SEQ ID NO: 32), or

QKCQRLQIEMNELLN (SEQ ID NO: 33), or

KCQRLQIEMNELLN (SEQ ID NO: 34), or

CQRLQIEMNELLN (SEQ ID NO: 35), or

QRLQIEMNELLN (SEQ ID NO: 36), or

RLQIEMNELLN (SEQ ID NO: 37), or

LQIEMNELLN (SEQ ID NO: 38), or

QIEMNELLN (SEQ ID NO: 39), or

IEMNELLN (SEQ ID NO: 40), or

EMNELLN (SEQ ID NO: 41), or

MNELLN (SEQ ID NO: 42), or

NELLN (SEQ ID NO: 43), or

ELLN (SEQ ID NO: 44), or

LLN, or

LN, or

N; and

Y2 is VATVISTAR (SEQ ID NO: 45), or

VATVISTA (SEQ ID NO: 46), or

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VATVIST (SEQ ID NO: 47), or

VATVIS (SEQ ID NO: 48), or

VATVI (SEQ ID NO: 49), or

VATV (SEQ ID NO: 50), or

VAT, or

VA, or

V, and

derivatives thereof having at least about 90% identity with SEEQ ID NO: 1 or SEQ ID NO: 2.

2(Amended). The peptide of claim 1 which is GVKETPQQKYQRLLHEVQELTTEVEKIKTTVKESATEEKLTPVXaaLAKQLAAL (SEQ ID NO: 51),

wherein Xaa is as defined in claim 1.

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Remarks

The amendments in the specification are of formal nature and serve to ensure conformation of the representations for the amino acids in the specification to the currently filed Sequence Listing. The amendments do not add new matter.

Attached hereto us a marked-up version of the changes made to the specification and claims by the current amendments. The attached page is <u>captioned "Version with markings to show changes made</u>."

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 30, 2001

Registration No. 33,055

Attorney of Record

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Sixteenth Floor

Newport Beach, CA 92660

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at page 3, line 21, has been amended as follows:

--In one aspect, the invention concerns an isolated peptide selected from the group consisting of:

(X1)_nEVEKIKTTVKESATEEKLTPV[X2]XaaL(X2)_m (SEQ ID NO: 1), (Y1)_nEVAALQVDRKVADEEKQSYDAV(Y2)_m (SEQ ID NO: 2),

wherein

n and m independently represent 0 or 1, and Xaa is V or L;

X1[, X2 and X3] and X2 are independently defined as follows

X1 is GVKETPQQKYQRLLHEVQELTT (SEQ ID NO: 3), or

VKETPQQKYQRLLHEVQELTT (SEQ ID NO: 4), or

KETPQQKYQRLLHEVQELTT (SEQ ID NO: 5) or,

ETPQQKYQRLLHEVQELTT (SEQ ID NO: 6) or,

TPQQKYQRLLHEVQELTT (SEQ ID NO: 7) or,

PQQKYQRLLHEVQELTT (SEQ ID NO: 8) or,

QQKYQRLLHEVQELTT (SEQ ID NO: 9) or,

QKYQRLLHEVQELTT (SEQ ID NO: 10) or,

KYQRLLHEVQELTT (SEQ ID NO: 11) or,

YQRLLHEVQELTT (SEQ ID NO:12) or,

QRLLHEVQELTT (SEQ ID NO: 13) or,

RLLHEVQELTT (SEQ ID NO: 14) or,

LLHEVQELTT (SEQ ID NO: 15) or,

LHEVQELTT (SEQ ID NO: 16) or,

HEVQELTT (SEQ ID NO: 17) or,

EVQELTT (SEQ ID NO: 18) or,

VQELTT (SEQ ID NO: 19) or,

QELTT (SEQ ID NO: 20) or,

ELTT (SEQ ID NO: 21), or

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            LTT, or
            TT, or
            T;
      [X2 is V or L,] and
      [X3] X2 is AKQLAAL (SEQ ID NO: 22), or
            AKQLAA (SEQ ID NO: 23), or
            AKQLA (SEQ ID NO: 24), or
            AKQL (SEQ ID NO: 25), or
            AKQ, or
            AK, or
            A;
and
      Y1 and Y2 are independently defined as follows
      Y1 is GEKETPVQKCQRLQIEMNELLN (SEQ ID NO: 26), or
            EKETPVQKCQRLQIEMNELLN (SEQ ID NO: 27), or
            KETPVQKCQRLQIEMNELLN (SEQ ID NO: 28), or
            ETPVQKCQRLQIEMNELLN (SEQ ID NO: 29), or
            TPVQKCQRLQIEMNELLN (SEQ ID NO: 30), or
            PVQKCQRLQIEMNELLN (SEQ ID NO: 31), or
            VQKCQRLQIEMNELLN (SEQ ID NO: 32), or
            QKCQRLQIEMNELLN (SEQ ID NO: 33), or
            KCQRLQIEMNELLN (SEQ ID NO: 34), or
            CQRLQIEMNELLN (SEQ ID NO: 35), or
            QRLQIEMNELLN (SEQ ID NO: 36), or
            RLQIEMNELLN (SEQ ID NO: 37), or
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LQIEMNELLN (SEQ ID NO: 38), or

QIEMNELLN (SEQ ID NO: 39), or

IEMNELLN (SEQ ID NO: 40), or

EMNELLN (SEQ ID NO: 41), or

MNELLN (SEQ ID NO: 42), or

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ELLN (SEQ ID NO: 44), or

LLN, or

LN, or

N; and

Y2 is VATVISTAR (SEQ ID NO: 45), or

VATVISTA (SEQ ID NO: 46), or

VATVIST (SEQ ID NO: 47), or

VATVIS (SEQ ID NO: 48), or

VATVI (SEQ ID NO: 49), or

VATV (SEQ ID NO: 50), or

VAT, or

VA, or

V, and

derivatives thereof having at least about 90% identity with SEQ ID NO: 1 or SEQ ID NO: 2.--

The paragraph beginning at page 5, line 31, has been amended as follows:

peptide has of the following preferred embodiment, the one --In sequences:GVKETPQQKYQRLLHEVQELTTEVEKIKTTVKESATEEKLTPV[X2]XaaLAKQ LAAL (SEO ID NO: 51), where [X2] Xaa is as defined above, or GEKETPVQKCQRLQIEMNELLNEVAALQVDRKVADEEKQSYDAVVATVISTAR (SEQ ID NO: 52), or has at least about 75%, preferably at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, most preferably at least about 95% identity with one of these sequences. Preferably, the peptide variants contain only conservative amino acid substitutions compared to the reference peptide sequences.--

The paragraph beginning at page 7, line 4, has been amended as follows:

--Figure 1 is the amino acid sequence of human p50 (SEQ ID NO: 53), wherein the peptide of SEQ ID NO: 51 ([X2] Xaa is L) is bolded and underlined.--

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The paragraph beginning at page 7, line 6, has been amended as follows:

-- Figure 2 is the partial amino acid sequence of mouse p50 (SEQ ID NO: 54), wherein the peptide of SEQ ID NO: 51 ([X2] Xaa is V) is bolded and underlined.--

In the claims:

Claims 1 and 2 have been amended as follows:

1(Amended). An isolated peptide selected from the group consisting of:

(X1)_nEVEKIKTTVKESATEEKLTPV[X2]XaaL(X2)_m (SEQ ID NO: 1),

(Y1), EVAALQVDRKVADEEKQSYDAV(Y2), (SEQ ID NO: 2),

wherein

n and m independently represent 0 or 1, and Xaa is V or L;

X1[, X2 and X3] and X2 are independently defined as follows

X1 is GVKETPQQKYQRLLHEVQELTT (SEQ ID NO: 3), or

VKETPQQKYQRLLHEVQELTT (SEQ ID NO: 4), or

KETPQQKYQRLLHEVQELTT (SEQ ID NO: 5) or,

ETPQQKYQRLLHEVQELTT (SEQ ID NO: 6) or,

TPQQKYQRLLHEVQELTT (SEQ ID NO: 7) or,

PQQKYQRLLHEVQELTT (SEQ ID NO: 8) or,

QQKYQRLLHEVQELTT (SEQ ID NO: 9) or,

QKYQRLLHEVQELTT (SEQ ID NO: 10) or,

KYQRLLHEVQELTT (SEQ ID NO: 11) or,

YQRLLHEVQELTT (SEQ ID NO:12) or,

QRLLHEVQELTT (SEQ ID NO: 13) or,

RLLHEVQELTT (SEQ ID NO: 14) or,

LLHEVQELTT (SEQ ID NO: 15) or,

LHEVQELTT (SEQ ID NO: 16) or,

HEVQELTT (SEQ ID NO: 17) or,

EVQELTT (SEQ ID NO: 18) or,

VQELTT (SEQ ID NO: 19) or,

QELTT (SEQ ID NO: 20) or,

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ELTT (SEQ ID NO: 21), or

LTT, or

T, or

T;

[X2 is V or L,] and

[X3] X2 is AKQLAAL (SEQ ID NO: 22), or

AKQLAA (SEQ ID NO: 23), or

AKQLA (SEQ ID NO: 24), or

AKQL (SEQ ID NO: 25), or

AKQ, or

AKQ, or

AK, or
```

and

A;

Y1 and Y2 are independently defined as follows

Y1 is GEKETPVQKCQRLQIEMNELLN (SEQ ID NO: 26), or EKETPVQKCQRLQIEMNELLN (SEQ ID NO: 27), or KETPVQKCQRLQIEMNELLN (SEQ ID NO: 28), or ETPVQKCQRLQIEMNELLN (SEQ ID NO: 29), or TPVQKCQRLQIEMNELLN (SEQ ID NO: 30), or PVQKCQRLQIEMNELLN (SEQ ID NO: 31), or VOKCQRLQIEMNELLN (SEQ ID NO: 32), or OKCORLQIEMNELLN (SEQ ID NO: 33), or KCQRLQIEMNELLN (SEQ ID NO: 34), or CQRLQIEMNELLN (SEQ ID NO: 35), or QRLQIEMNELLN (SEQ ID NO: 36), or RLQIEMNELLN (SEQ ID NO: 37), or LQIEMNELLN (SEQ ID NO: 38), or QIEMNELLN (SEQ ID NO: 39), or IEMNELLN (SEQ ID NO: 40), or EMNELLN (SEQ ID NO: 41), or MNELLN (SEQ ID NO: 42), or

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NELLN (SEQ ID NO: 43), or

ELLN (SEQ ID NO: 44), or

LLN, or

LN, or

N; and

Y2 is VATVISTAR (SEQ ID NO: 45), or

VATVISTA (SEQ ID NO: 46), or

VATVIST (SEQ ID NO: 47), or

VATVIS (SEQ ID NO: 48), or

VATVI (SEQ ID NO: 49), or

VATV (SEQ ID NO: 50), or

VAT, or

VA, or

V, and

derivatives thereof having at least about 90% identity with SEEQ ID NO: 1 or SEQ ID NO: 2.--

2(Amended). The peptide of claim 1 which is GVKETPQQKYQRLLHEVQELTTEVEKIKTTVKESATEEKLTPV[X2]XaaLAKQLAAL

(SEQ ID NO: 51),

wherein [X2] Xaa is as defined in claim 1.

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